

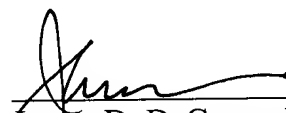
REMARKS

As is stated in the accompanying Statement under 37 C.F.R. §§ 1.821-1.825, Applicants amend the application to include a Sequence Listing in accordance with the sequence rules. This Sequence Listing includes all nucleic acid and amino acid sequences disclosed in the specification. In addition, Applicants amend the specification to refer to all sequences by their respective sequence identifiers. Applicants submit that these amendments contain no new matter.

Enclosed are clean and "marked-up" versions of the replacement paragraphs. If there are any charges or any credits, please apply them to Deposit Account No. 03-2095.

Respectfully submitted,

Date: September 24, 2002


James D. DeCamp, Ph.D.
Reg. No. 43,580

Clark & Elbing LLP
101 Federal Street
Boston, MA 02110-2106
Telephone: 617-428-0200
Facsimile: 617-428-7045
07678.062004 Amendment.dot



21559
PATENT TRADEMARK OFFICE



U.S. Serial No. 09/613,486

Version of Replacement Paragraphs Showing Changes Made,

Pursuant to 37 C.F.R. § 1.121(b)(1)(iii)

Amend the paragraph beginning on page 9, line 18, as follows.

Figure 3A-3D are comparisons between ORF1a/ORF1b of GLRaV-2 and BYV. Figure 3A-3D show the conserved domains of two papain-like proteases (P-PRO), methyltransferase (MT/MTR), helicase (HEL), and RNA-dependent RNA polymerase (RdRP), respectively (SEQ ID NOS: 3, 5, and 24-27). Exclamation marks indicate the predicted catalytic residues of the leader papain-like protease; slashes indicate the predicted cleavage sites. The conserved motifs of the MT, HEL, and RdRP domains are highlighted with overlines marked with respective letters. The alignment is constructed using the MegAlign program in DNASTAR.

Amend the paragraph beginning at page 9, line 25, as follows.

Figures 4A and 4B are alignments of the nucleotide (Figure 4A) and deduced amino acid (Figure 4B) sequences of ORF1a/ORF1b overlapping region of GLRaV-2, BYV, BYSV, and CTV (SEQ ID NOS: 28-35). Identical nucleotides and amino acids are shown in consensus. GLRaV-2 putative + 1 frameshift site (TAGC) and its corresponding sites of BYV (TAGC) and BYSV (TAGC) and CTV (CGGC) at nucleotide and amino acid sequences are highlighted with underlines.

Amend the paragraph beginning at page 9, line 31, as follows.

Figure 5 is an alignment of the amino acid sequence of HSP70 protein of GLRaV-2 and BYV (SEQ ID NOS: 9 and 36). The conserved motifs (A to H) are indicated with overlines and marked with respective letters. The alignment was conducted with the MegAlign program of DNASTAR.

Amend the paragraph beginning at page 10, line 3, as follows.

Figure 6A is a comparison of the coat protein (CP) and coat protein duplicate (CPd) of GLRaV-2 with other closteroviruses (SEQ ID NOS: 13, 15, and 37-42). The amino acid sequence of the GLRaV-2 CP and CPd are aligned with the CP and CPd of BYV, BYSV, and CTV. The conserved amino acid residues are in bold and the consensus sequences are indicated. Sequence alignment and phylogenetic tree were constructed by Clustal Method in the MegAlign Program of DNASTAR. Figure 6B is a tentative phylogenetic tree of the CP and CPd of GLRaV-2 with BYV, BYSV, CTV, LIYV, LChV, and GLRaV-3. To facilitate the alignment, only the C-terminal 250 amino acids of CP and CPd of LIYV, LChV, and GLRaV-3 were used. The scale beneath the phylogenetic tree represents the distance between sequences. Units indicate the number of substitution events.

Amend the paragraph beginning at page 10, line 20, as follows.

Figure 9 is an alignment of the amino acid sequence of HSP90 protein of GLRaV-2 with respect to other closteroviruses, BYS, BYSV, and CTV (SEQ ID NOS: 11 and 43-45). The most conserved motifs (I to II) are indicated with the highlighted lines and marked with respective letters.

Amend the paragraph beginning at page 10, line 23, as follows.

Figure 10 is an alignment of the nucleotide sequence of 3'-terminal untranslated region of GLRaV-2 with respect to the closteroviruses BYV (Agranovsky et al., "Beet Yellows Closterovirus: Complete Genome Structure and Identification of a Papain-like Thiol Protease," Virology 198:311-24 (1994), which is hereby incorporated by reference), BYSV (Karasev et al., Organization of the 3'-Terminal Half of Beet Yellow Stunt Virus Genome and Implications for the Evolution of Closteroviruses," Virology 221:199-207 (1996), which is hereby incorporated by reference), and CTV (Karasev et al., "Complete Sequence of the Citrus Tristeza Virus RNA Genome," Virology 208:511-20 (1995), which is hereby incorporated by reference) (SEQ ID NOS: 1 and 46-48). The consensus sequences are shown, and the distance to the 3'-end is indicated. A complementary region capable of forming a "hair-pin" structure is underlined.

Clean Version of the Replacement Paragraphs,

Pursuant to 37 C.F.R. § 1.121 (b)(1)(ii)

Figure 3A-3D are comparisons between ORF1a/ORF1b of GLRaV-2 and BYV. Figure 3A-3D show the conserved domains of two papain-like proteases (P-PRO), methyltransferase (MT/MTR), helicase (HEL), and RNA-dependent RNA polymerase (RdRP), respectively (SEQ ID NOS: 3, 5, and 24-27). Exclamation marks indicate the predicted catalytic residues of the leader papain-like protease; slashes indicate the predicted cleavage sites. The conserved motifs of the MT, HEL, and RdRP domains are highlighted with overlines marked with respective letters. The alignment is constructed using the MegAlign program in DNASTAR.

Figures 4A and 4B are alignments of the nucleotide (Figure 4A) and deduced amino acid (Figure 4B) sequences of ORF1a/ORF1b overlapping region of GLRaV-2, BYV, BYSV, and CTV (SEQ ID NOS: 28-35). Identical nucleotides and amino acids are shown in consensus. GLRaV-2 putative + 1 frameshift site (TAGC) and its corresponding sites of BYV (TAGC) and BYSV (TAGC) and CTV (CGGC) at nucleotide and amino acid sequences are highlighted with underlines.

Figure 5 is an alignment of the amino acid sequence of HSP70 protein of GLRaV-2 and BYV (SEQ ID NOS: 9 and 36). The conserved motifs (A to H) are indicated with overlines and marked with respective letters. The alignment was conducted with the MegAlign program of DNASTAR.

Figure 6A is a comparison of the coat protein (CP) and coat protein duplicate (CPd) of GLRaV-2 with other closteroviruses (SEQ ID NOS: 13, 15, and 37-42). The amino acid sequence of the GLRaV-2 CP and CPd are aligned with the CP and CPd of BYV, BYSV, and CTV. The conserved amino acid residues are in bold and the consensus sequences are indicated. Sequence alignment and phylogenetic tree were constructed by Clustal Method in the MegAlign Program of DNASTAR. Figure 6B is a tentative phylogenetic tree of the CP and CPd of GLRaV-2 with BYV, BYSV, CTV, LIYV, LChV, and GLRaV-3. To facilitate the alignment, only the C-terminal 250 amino acids of CP and CPd of LIYV, LChV, and GLRaV-3 were used. The scale beneath the phylogenetic tree represents the distance between sequences. Units indicate the number of substitution events.

Figure 9 is an alignment of the amino acid sequence of HSP90 protein of GLRaV-2 with respect to other closteroviruses, BYS, BYSV, and CTV (SEQ ID NOS: 11 and 43-45). The most conserved motifs (I to II) are indicated with the highlighted lines and marked with respective letters.

Figure 10 is an alignment of the nucleotide sequence of 3'-terminal untranslated region of GLRaV-2 with respect to the closteroviruses BYV (Agranovsky et al., "Beet Yellows Closterovirus: Complete Genome Structure and Identification of a Papain-like Thiol Protease," Virology 198:311-24 (1994), which is hereby incorporated by reference), BYSV (Karasev et al., Organization of the 3'-Terminal Half of Beet Yellow Stunt Virus Genome and Implications for the Evolution of Closteroviruses," Virology 221:199-207 (1996), which is hereby incorporated by reference), and CTV (Karasev et al., "Complete Sequence of the Citrus Tristeza Virus RNA Genome," Virology 208:511-20 (1995), which is hereby incorporated by reference) (SEQ ID NOS: 1 and 46-48). The consensus sequences are shown, and the distance to the 3'-end is indicated. A complementary region capable of forming a "hair-pin" structure is underlined.